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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/718,425	11/24/2000	Oren Becker	24460	1582

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EXAMINER
MARSCHEL, ARDIN H

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/718,425	BECKER ET AL.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1631.

Applicants' arguments, filed 1/8/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

DRAWINGS

Applicant is hereby notified that the required timing for the correction of drawings has changed. See the last 6 lines on the sheet which is attached entitled "Attachment for PTO-948 (Rev. 03/01 or earlier)". It is noted that a PTO Form 948 is mailed herewith. Due to the above notification Applicant is required to submit drawing corrections within the time period set for responding to this Office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

SEQUENCE RULES NON-COMPLIANCE

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR §§1.821(a)(1) and (a)(2). See, for example, the Zif268 sequence on page 18 in Table 1 of the instant specification. See also the sequences in Table 2A on page 21, Table 3 on page 24, Table 4 on page 28. This application fails to comply with the requirements of

37 CFR §§ 1.821 through 1.825 because it lacks any submission of a computer readable form sequence listing, a paper copy for the specification, a statement under 37 CFR §§ 1.821(f) and (g), and SEQ ID Nos cited along with each sequence in the specification. Applicants are also reminded that a CD-ROM sequence listing submission may replace the paper and computer readable form sequence listing copies. Applicant(s) are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office action.

IMPROPER CLAIM NUMBERING

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 32 been renumbered claim 23.

LACK OF UTILITY

The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.

The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-17, 22, and 23 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The claimed subject matter is not supported by a specific, substantial, and credible utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter

would be required to identify or reasonably confirm a "real world" use. The examiner does not find an adequate nexus between the evidence of record and the asserted properties of the claimed subject matter.

Applicants should explicitly identify a specific, substantial, and credible utility for the claimed invention and establish a probative relation between any evidence of record and the originally disclosed properties of the claimed invention.

The claimed invention lacks either specific or substantial utility. Reconsideration of the instant claims reveals that a method is set forth for the prediction of an amino acid sequence which is constructed via evaluation of solvent accessibility without any specific or substantial utility for the predicted protein or peptide. In part a of claim 1 a 3D structure is set provided but without any specificity as to a connection to a utility for the structure. That is, there is no required substrate binding activity set forth. Alternatively, there is no recognition of a binding entity present as a claimed limitation nor set forth in the instant specification. Additionally, the solvent accessibility which is utilized in the claimed method to be compatible with the solvent accessibility at each position is not directed to a protein or peptide utility. Thus, a generic utility is apparently meant for the protein or peptide being predicted as to its amino acid sequence. A generic utility is not specific as required by 35 U.S.C. § 101. There is also a lack of a substantial utility as there is no substantial utility defined or even asserted for the predicted protein or peptide sequence as a result of performance of the methods as claimed either for enzyme activity or some type of binding or recognition activity such as present in proteins or peptides which act as receptors, for example, or possibly peptides

which bind to receptors in order to produce some type of biological response for said binding. It is noted that claim 2 includes a native protein as an option for providing the 3D structure for part (a) of claim 1. Nothing specific or substantial is therein set forth as to such a native protein, but rather a general or generic protein is set forth without further limitation regarding utility thereof thus additionally supporting this determination of a lack of specific or substantial utility. It may be postulated that the solvent accessibility is somehow related to protein or peptide utility in step c of instant claim 1. This, however, is not asserted as defining a utility for the practice of step c in the instant specification nor in the claims such that the solvent accessibility results in some type of protein or peptide utility. It is acknowledged that one aspect of a protein's or peptide's function includes solvent accessibility for binding activity, but that such solvent accessibility per se lacks specificity as to what binding then occurs for entities which have access via solvent accessibility. Is hydrogen bonding then utilized via such accessibility? Is there ionic bonding? Are other types of interaction/.bonding then utilized for protein or peptide function or activity? At best solvent accessibility provides access but does not produce whatever interactions or bond availability thus results in a protein or peptide activity or function. Thus, the utility of predicting an amino acid sequence for a protein or peptide as instantly claimed lacks specificity or substantiality as to utility without some nexus to protein or peptide activity or binding reactions which will result in specific and substantial utility. It is noted that no well established utility has been asserted or is known for generic amino acid sequence prediction without some utility for the resultant protein or peptide. It is also noted that, in the absence of a well

known utility, a utility must be substantiated which has the combination of specific, substantial, and credible utility. Since the instant invention as disclosed lacks either specific or substantial utility, the credibility is not required to be assessed. That being stated, it is acknowledged that protein or peptide design per se is deemed a credible utility for proteins or peptides with some function or activity which has both a specific and substantial use.

LACK OF ENABLEMENT

Claims 1-17, 22, and 23 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 22, and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at

1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

In the practice of the instant claims, the construction of a "reduced" virtual representation is required for step b of claim 1, and all dependent claims due to their dependence directly or indirectly from claim 1. This construction of a "reduced" virtual representation is essential subject matter for the performance of this step in the instantly claimed method. Consideration of the instant disclosure reveals that a publication is apparently incorporated by reference to set forth the details of such a "reduced" virtual representation on page 9, lines 4-6. It is noted that the specification on page 9, lines 7-27, sets forth some concepts in this virtual representation but never discloses with any significant details as to how this is performed in the claimed invention regarding coordinates as provided firstly in step a of instant claim 1. Thus, reliance on said printed publication on page 9, lines 4-6, for this practice is apparent thus also making this printed publication essential subject matter for the practice of the instant claims. The incorporation of essential subject matter via incorporation by reference to a printed

publication is improper as also explained in the following paragraph and thus lacking in enablement.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

VAGUENESS AND INDEFINITENESS

Claims 1-17, 22, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, step d, the "compatible" limitation causes this claim and those dependent therefrom to be vague and indefinite as there is no instant definition of what the metes and bounds of this limitation are. Does compatible indicate that the solvent accessibility is the same? Does it indicate that it is similar without defining a spatial similarity limit? Such comparative limitations are vague and indefinite unless some definition of what the comparison limits are. Clarification is requested via clearer claim wording.

The antecedent basis for "each position" in claim 1, step c is vague and indefinite and causes claims dependent from claim 1 to also contain this unclarity. Does this indicate each amino acid position in the backbone of step a given some putative protein or peptide such as listed in claim 2 to start with? The claim does not clearly and concisely point to amino acids as defining "each position" in step c. Could the positions for "each position" be defined by solvent accessibility surfaces in the "undefined" starting backbone of step a? Clarification via clearer claim wording is requested.

In claim 1, step d, a conflict exists between the first 2 lines of this step and the last 2 lines of step d. In the first line a random amino acid sequence is assigned, but then in the last 2 lines non-random amino acid selection apparently is set forth via a solvent accessibility requirement. These random vs. non-random practices conflict. Clarification via clearer claim wording is requested.

In claim 1, part iv, a determination is set forth for accepting or rejecting a mutation but without any definition of the metes and bounds of what determines the acceptance or rejection. Clarification via clearer claim wording is requested.

PRIOR ART REJECTIONS

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9-17, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Dahiyat et al. (Protein Science, 1996, Vol. 5, pages 895-903).

This rejection is maintained and reiterated from the previous office action, mailed 8/9/02, and claim 23 is added as being directed to computer practices which are suggested as also well known for such computers for automation as noted in the title of Dahiyat et al., for example. Applicants argue firstly that the reference does not utilize a "reduced" virtual representation set. In response the abstract of the reference discloses steric complementarity using a van der Waals potential. This is a disclosure of a type of reduced representation of the rotamers as described in the reference over other representations such as utilizing electron orbitals or other complex quantum mechanical representations contrary to the arguments of applicants. Applicants further argue that the reference does not utilize solvent accessibility as a design parameter. In response the previous office action clearly set forth the designing of protein from surface area burial, buried atoms, hydrophobic and hydrophilic positions which are solvent accessibility determinations again contrary to the arguments of applicants. Applicants then argue a lack of Monte-Carlo search algorithms in the reference. Again in response the usage of Monte-Carlo algorithms for sequence searching was noted in said previous office action on page 897 of the reference contrary to applicants' argument. In summary all of applicants' arguments are non-persuasive as being contrary to the factual basis for this rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahiyat et al. (Protein Science, 1996, Vol. 5, pages 895-903), and further in view of Hurley et al. (JMB Vol. 224, 1992, pages 1143-1159).

This rejection is reiterated and maintained from the previous office action, mailed 8/9/02, but additionally applied to claims 1-5, 9-17, 22, and 23 as the embodiments in claims 6-8 as previously rejected are deemed embodiments within claims 1-5, 9-17, 22, and 23 as being recited in claims 6-8. Applicants argue the lacking descriptions in Dahiyat et al. These arguments directed to Dahiyat et al. have been responded to above as being non-persuasive and are reiterated here as being equally non-persuasive and responded to as noted above. Applicants additionally argue that Hurley et al. does not remedy the lacking descriptions in Dahiyat et al. In response, Dahiyat does not lack what applicants allege and thus Hurley et al. does not need to remedy that for which no remedy is required. Applicants then argue that the energy evaluation in Hurley et al. is limited to particular residues and also utilizes a different energy evaluation method than

that as instantly claimed. In response, the instant claims are not limited as to what portion of the sequence is evaluated as to energy scoring, either buried or solvent accessible thus making this argument be directed to a instant claim limitation which is not present in the instant claims. Further, the instant claims do not limit the particular energy scoring methodology and thus that utilized in Hurley et al. is deemed to be within that of the generic energy scoring practice of the instant claims. Thus, the arguments of applicants are non-persuasive.

INFORMALITIES

The disclosure is objected to because of the following informalities:

Claim 1 contains improper internal periods. The periods, for example, in the part "a." or "b.", etc. designation in claim 1 are improper. Claim 23 also contains improper periods. Periods are only permitted within a claim in abbreviations and at the end. Applicants are suggested to replace the part designation periods with parentheses, for example.

Appropriate correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

May 8, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER